Quiz two will be on Tuesday November 23rd

MHC class 2 molecules and T lymphocyte Help

Immunology lecture 20
November 18th 2010
Structure of Class II Antigens

α peptide chain
32,000 daltons

β peptide chain
28,000 daltons

H₂N

α₁ β₁

β₂

Carbohydrate

Found on B-lymphocytes, monocytes, macrophages, epithelial cells, and spermatozoa.

Membrane
Class I molecule

Peptide-binding cleft

Class II molecule

Membrane-distal domains

Membrane-proximal domains (Ig-fold structure)

Transmembrane segment

Cytoplasmic tail

α₂

α₁

α₃

β₂-microglobulin

β₁

β₂
(a) TCR–peptide–class I MHC  (b) TCR–peptide–class II MHC
Peptides in MHC2 can slide across binding region to fit.
Interaction with Antigen

MHC Class I - bound peptide

- \( \alpha_1 \)-Helix
- Peptide
- \( \alpha_2 \)-Helix

MHC Class II - bound peptide

- DR\( \alpha \)-chain
- Peptide
- DR\( \beta \)-chain

Companions
MHC
Class II
8-10

13-18
upto 34
So how do peptides get into MHC1 and MHC2 class molecules?

• Class 1 molecules use the Endogenous pathway.
• Class 2 molecules use the Exogenous pathway.
No infection on a normal day....
CD8+ T cell

murdered cell
Third method of Cytotoxic T cell killing:

1. CTL recognizes antigen on target cell
2. CTL is activated
3. A lethal hit is delivered by the CTL using agents such as perforin or granzyme B
4. The CTL detaches from the target cell
5. Target cell dies by apoptosis
cytotoxic T cell

FIGURE 1: Tumor cell
First method of cytotoxic T cell killing of target cells
MHC 2 molecules on surface

- Everyday MHC 2 molecules produced and transported to the membrane of antigen presenting cells.
- What does this look like on a good day when there is no infection .....
B cell,
Macrophage
Dendritic cell
not in the
presence of
antigen.
What if B cells binds antigen?
What if dendritic cell pinocytoses antigen?
What if macrophage phagocytosis antigen?

Antigen is internalized, processed and presented on the surface of the cell bound to MHC 2 molecules and can be recognized only by CD 4+ T helper cells
ENDOCYTIC PATHWAY

Exogenous antigens → Endocytic compartments → Peptides → Peptide-class II MHC complex

Endocytosis or phagocytosis
**Figure 5-2 Immunobiology**

<table>
<thead>
<tr>
<th>Intravesicular pathogens</th>
<th>Extracellular pathogens and toxins</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endocytic vesicles</strong> (low pH)</td>
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</tr>
<tr>
<td>MHC class II</td>
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</tr>
<tr>
<td>CD4 T cells</td>
<td>CD4 T cells</td>
</tr>
<tr>
<td>Activation to kill intravesicular bacteria and parasites</td>
<td>Activation of B cells to secrete Ig to eliminate extracellular bacteria/toxins</td>
</tr>
</tbody>
</table>
B- lymphocyte as a antigen presenting cell

- Antigen
- Clathrin-coated vesicle
- Early endosome pH 6.0-6.5
- Recycling of receptors
- Late endosome pH 5.0-6.0
- Lysosome pH 4.5-5.0
- Golgi complex
- 1st
- 2nd
Dendritic cells, macrophages, monocytes.
While in RER, MHC2 being made
While in the cell, antigen is being internalized
Acidification of vesicles activates proteases to degrade antigen into peptide fragments

Vesicles containing peptides fuse with vesicles containing MHC class II molecules
Antigen-presenting cell

MHC II

MHC class II

Antigen fragment

CD4

TCR

Helper T cell

T_h
MACROPHAGE

BACTERIAL CELL BEING ENGULFED

ANTIGEN DISPLAYED ON SURFACE AFTER DIGESTION

T-HELPER CELL BEING ACTIVATED
The T helper (Th)-cell and phagocytic response to tumour cells
T cells are MHC restricted. They only help or kill cells with whom they share MHC.
Helper T cells are also MHC restricted.
This work indicated that T cells recognize both MHC and specific antigen fragments.

Does one receptor recognize the MHC and another receptor recognize the antigen fragment embedded in the binding site on the MHC? Or is there one receptor with specificity for MHC in combination with a specific antigen fragment?
Dual Receptor Theory

<table>
<thead>
<tr>
<th>Antigen</th>
<th>MHC on APCs</th>
<th>Expected response</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVA</td>
<td>IA$^k$</td>
<td>Dual-receptor model +</td>
</tr>
<tr>
<td>OVA</td>
<td>IA$^f$</td>
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</table>
Experiment demonstrating the thymus selects this MHC specificity.
T cell differentiation in the thymus
Erythrocytes Monocytes Granulocytes Lymphocytes Megakaryocytes

Thymus processing

T-lymphocyte

Lymphoblasts

Cell-mediated reaction

Antigen Stimulation

Clones of T Cells in Secondary Lymphoid Organs

Bone marrow stem cells

"Bursa" processing

B-Lymphocyte

Plasma cells

Humoral antibody synthesis

Secondary Organs
1. Spleen
2. Lymph Nodes
3. Peyer's Patches
4. Appendix

Co-operation

Cytokine cytotoxin

Antibody

Clones of B Cells in Secondary Lymphoid Organs

Cells are carried by the blood to Secondary lymphoid organs
T cell differentiation: How to explain MHC restriction and double the number of T helper cells compared to cytotoxic cells.